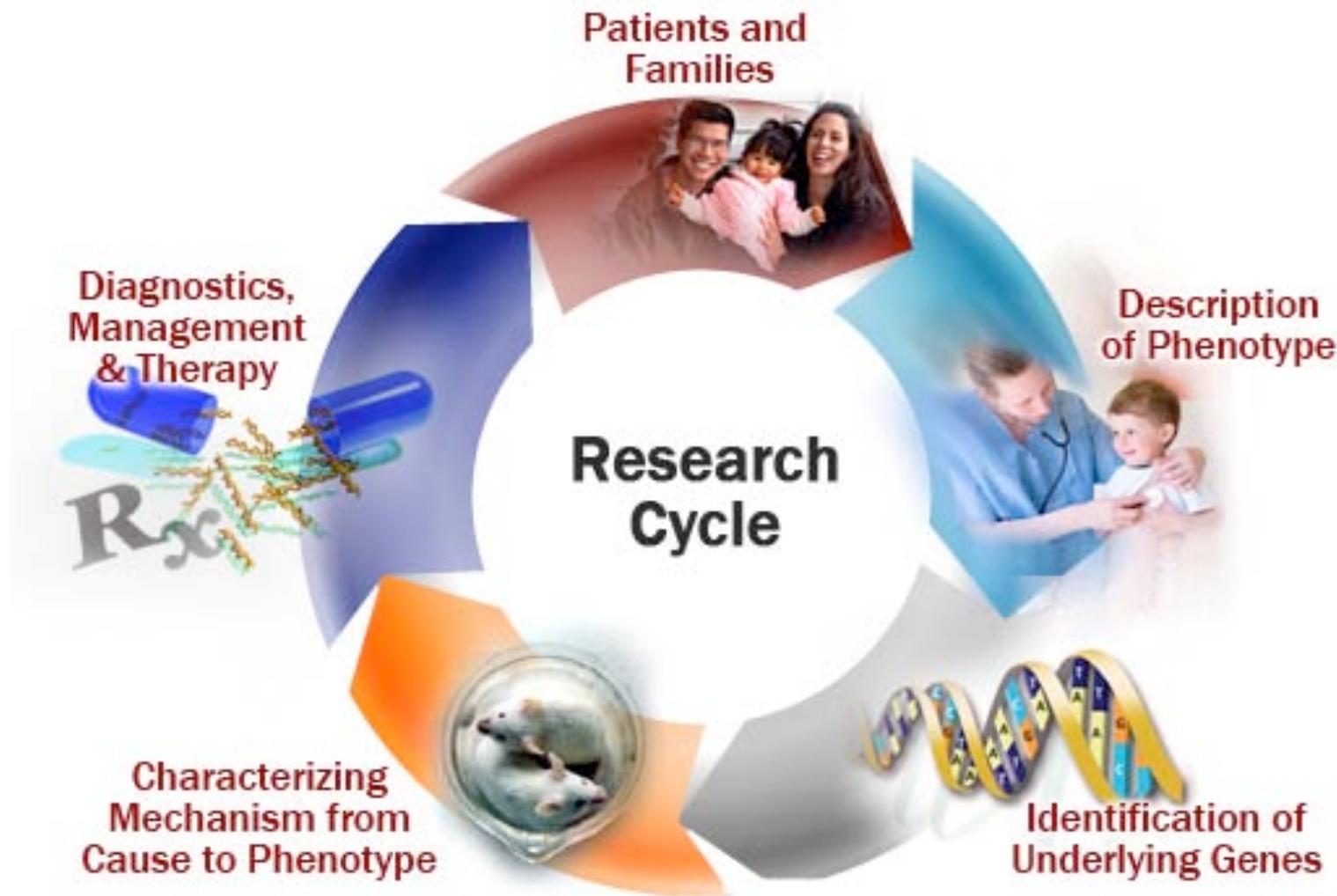
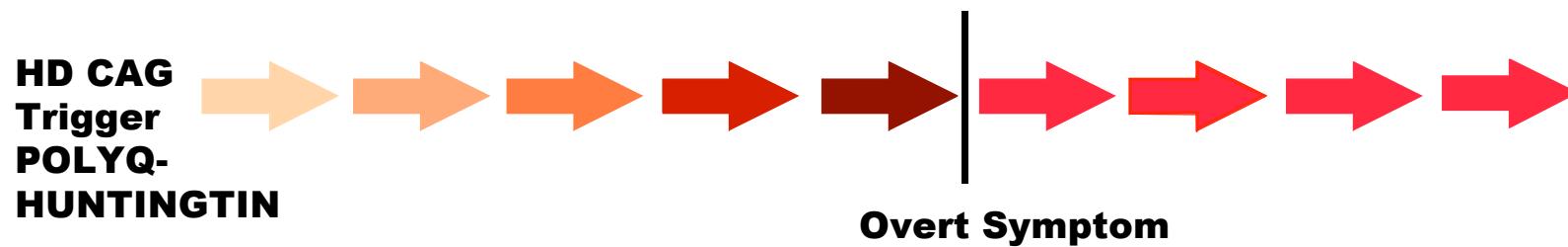


HDSA RESEARCH PARTNERSHIP

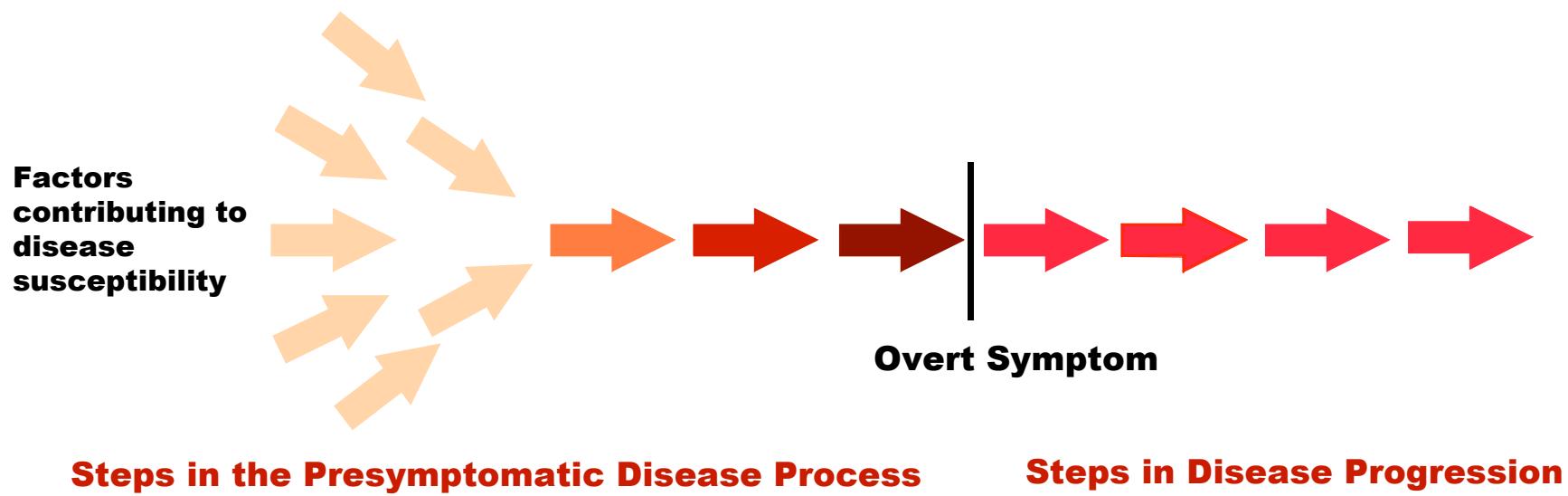


Pathogenesis and clinical disease



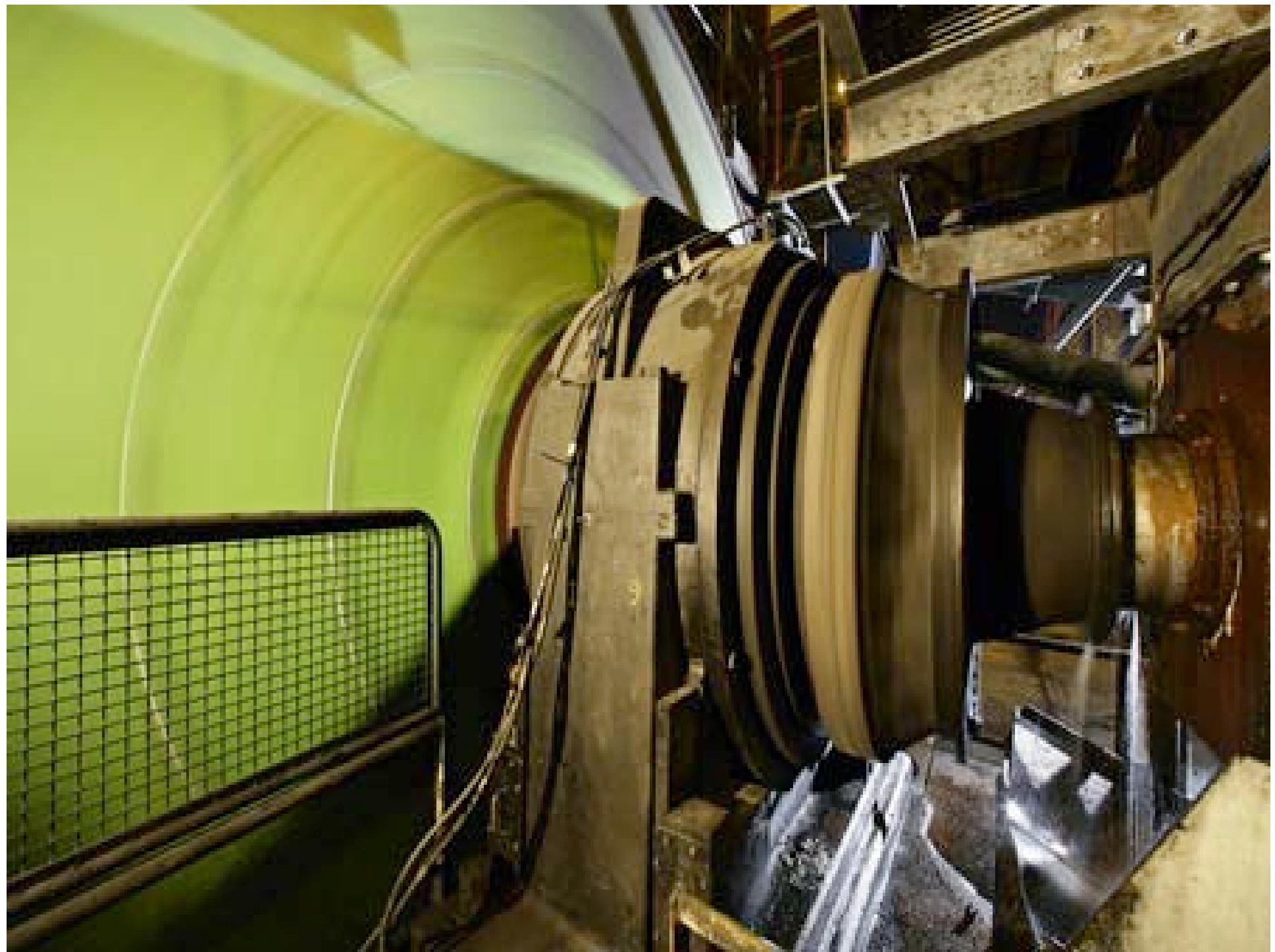
Steps in the Presymptomatic Disease Process

Steps in Disease Progression









gettyimages®







Huntington's Disease
Society of America

HDSA Research Pipeline to Treatments

Discovery Research

Flexibility
variety of strategies

Identify
possible treatment

Applied Research

Optimize
possible treatment

Clinical Trial Research

Preclinical
testing-
'model
systems'

Phase 1
Clinical Trial

Phase 2
Clinical Trial

Phase 3
Clinical Trial



Target



**FDA
approved
drug**

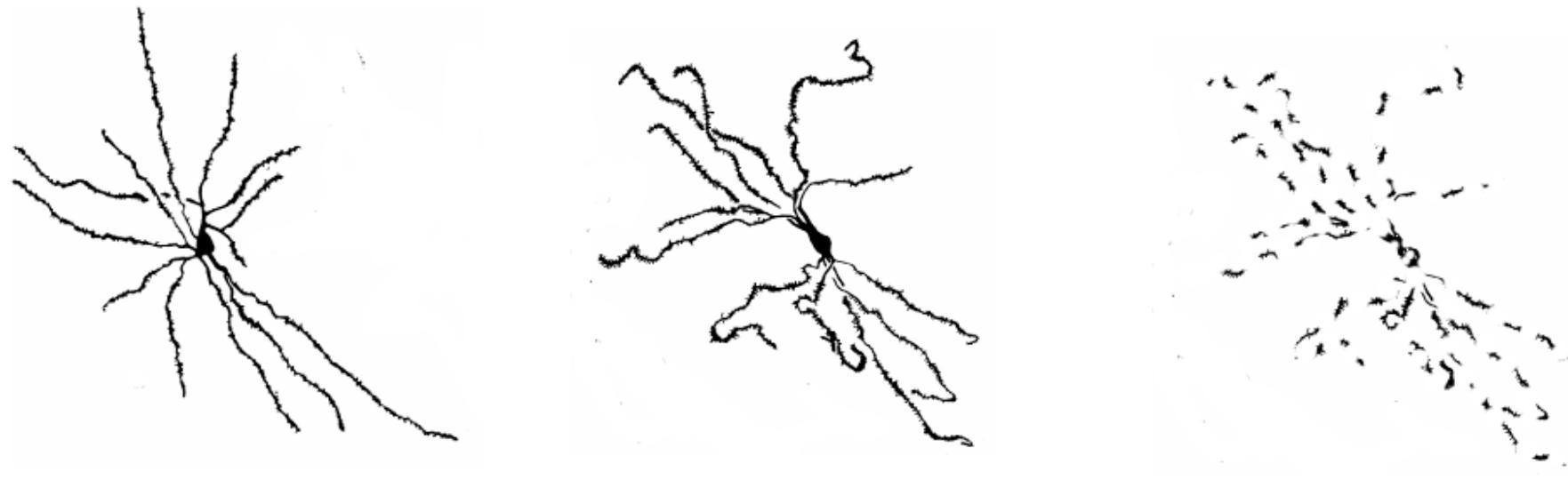
**Change
due to the
HD gene**



Discovery
Start with the right ore

**Grants and Fellowships
Coalition**





Mutant huntingtin → → → → → → → **Death**

Lifeline of a brain cell with the HD mutation

Trigger mechanism

Changes that disable the brain cell

Changes that kill the brain cell

Focus of HDSA Research

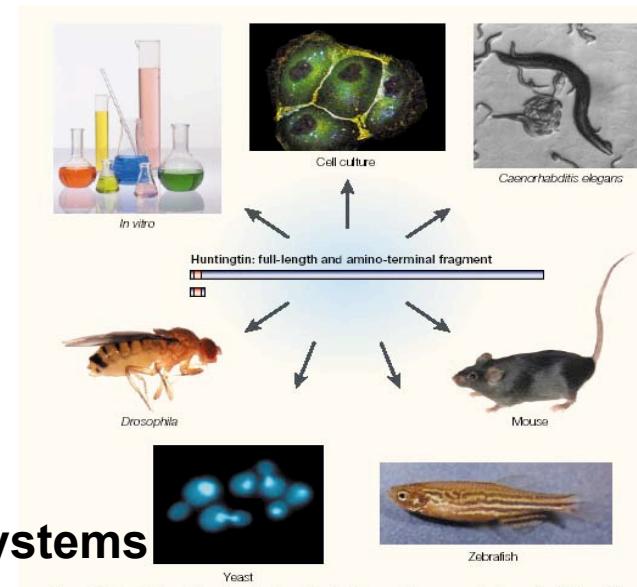
Grants and Fellowships

NEW IDEAS, NEW (DEDICATED) HD RESEARCHERS

- **Vital flexible funding to seed new HD research areas and to support young researchers at the start of their careers**
- **Grant \$50,000 for one year**
- **Fellowship \$40,000 per year (2 years)**



Huntingtin protein



Grant Recipient



Dr. Ruth Luthi-Carter, Ph.D.
Swiss Federal Institute of Technology
Lausanne Switzerland
Molecular changes in human HD brain

Fellowship Recipients



Dr. Brownen Martin, Ph.D.
National Institutes of Health (Bethesda MD)
Molecules that respond to sugar



Dr. Jean Savare, Ph.D.
J. David Gladstone Institutes (San Francisco CA)
Finding all huntingtin partners in yeast



Dr. Austin Milnerwood, Ph.D. (with HSC)
University British Columbia
Brain cell function in YAC128 HD gene mice

Coalition

16 expert international laboratories committed to cooperative HD research, self-organized into teams aimed at pressing issues in HD research, closely aligned with HSC, CHDI, NIH in order to capitalize quickly on the research findings.

Gillian Bates, Ph.D.

Flint Beal, M.D.

David Borchelt, Ph.D.

Elena Cattaneo, Ph.D.

Jang-Ho Cha, M.D., Ph.D.

Marian Difiglia, Ph.D.

Robert Freedlander, M.D.

James Gusella, Ph.D.

Michael Hayden, M.D., Ph.D.

Steven Hersch, M.D., Ph.D.

Ron Kopito, Ph.D.

Marcy MacDonald, Ph.D.

Richard Morimoto, Ph.D.

Christopher Ross, M.D., Ph.D.

Leslie Thompson, Ph.D.

Erich Wanker, Ph.D.

Huntingtin - a cargo barge

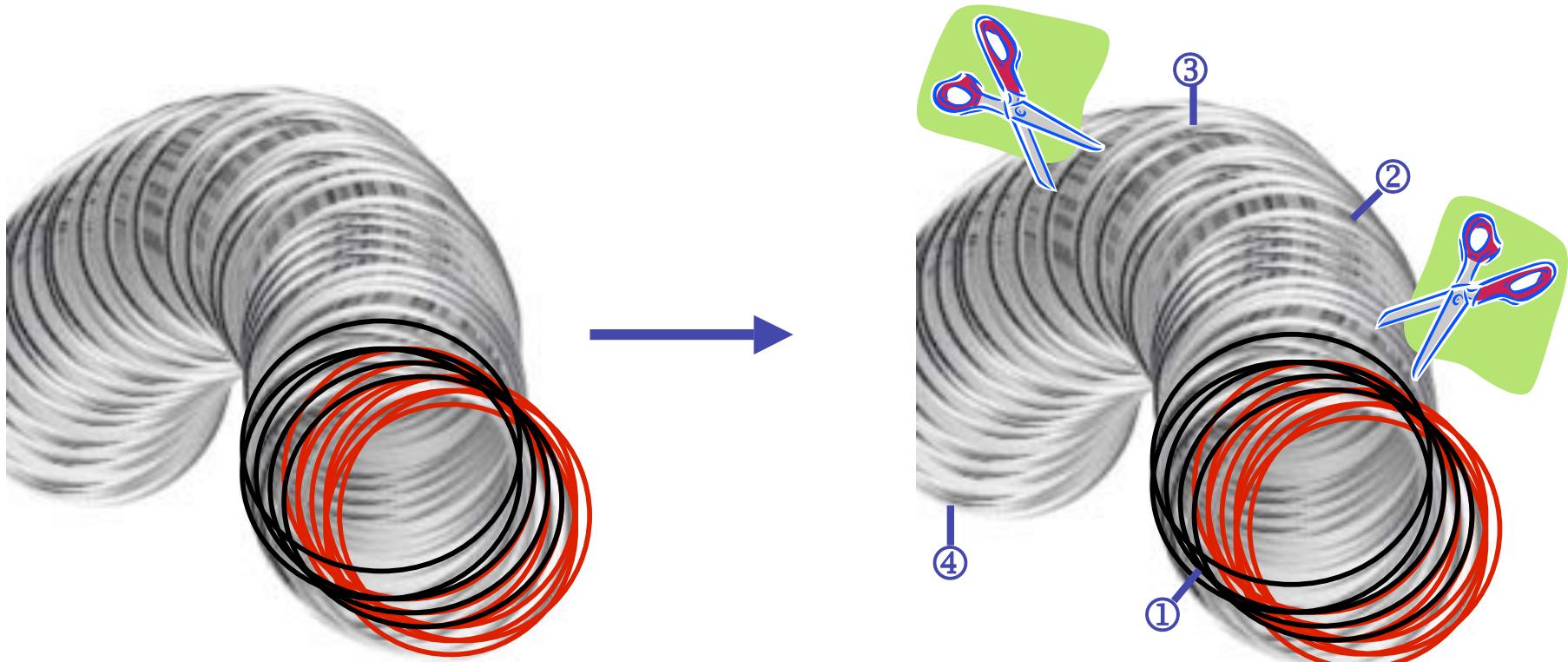


Barge A-390 & Tug, Lake St. Clair, 9/26/2002
Don Coles, Great Lakes Aerial Photos

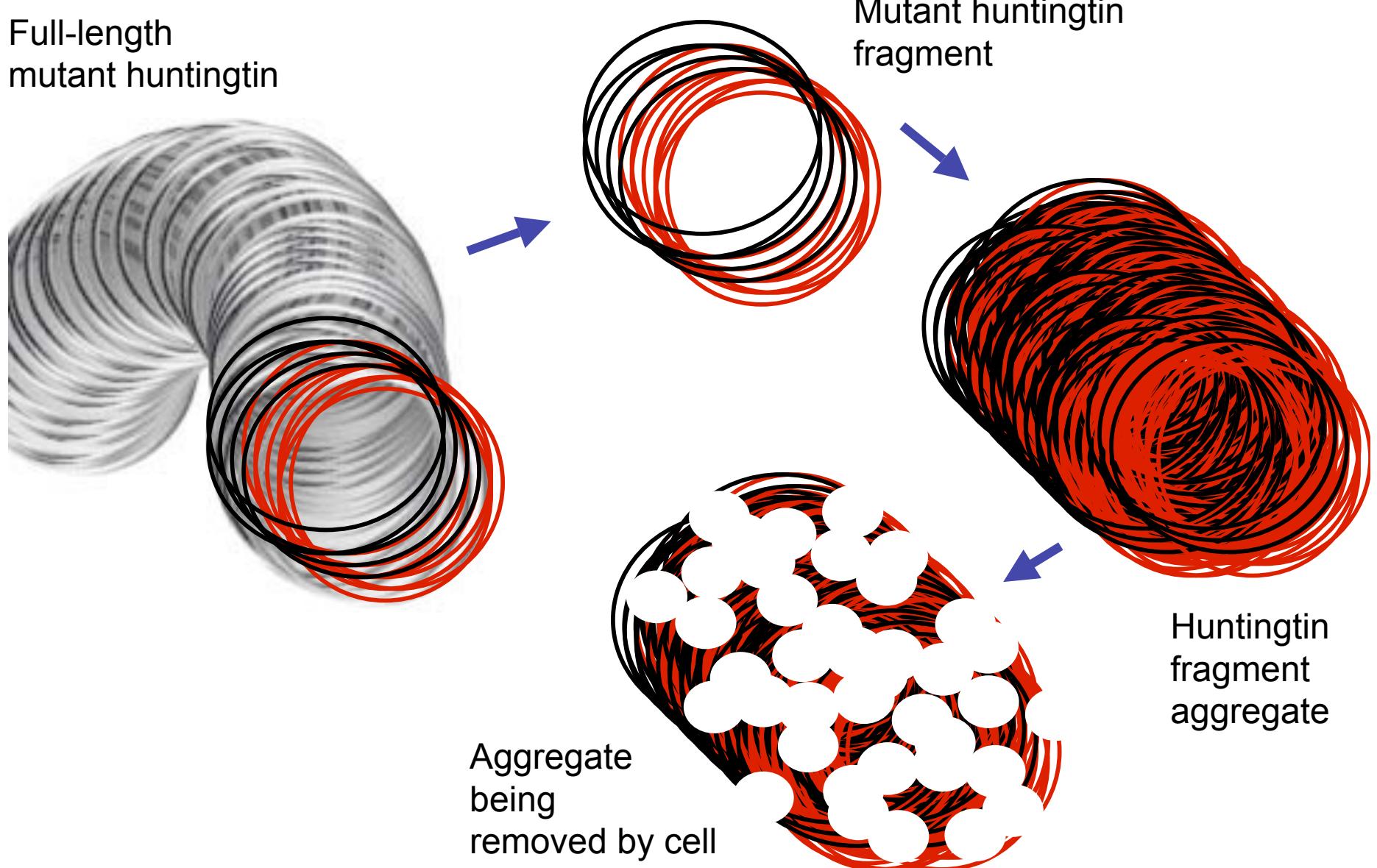
Huntingtin Function



Mitochondria & Energy Metabolism



Huntingtin Proteolysis and Posttranslational Modification



Folding, Aggregation and Clearance of Mutant Huntingtin

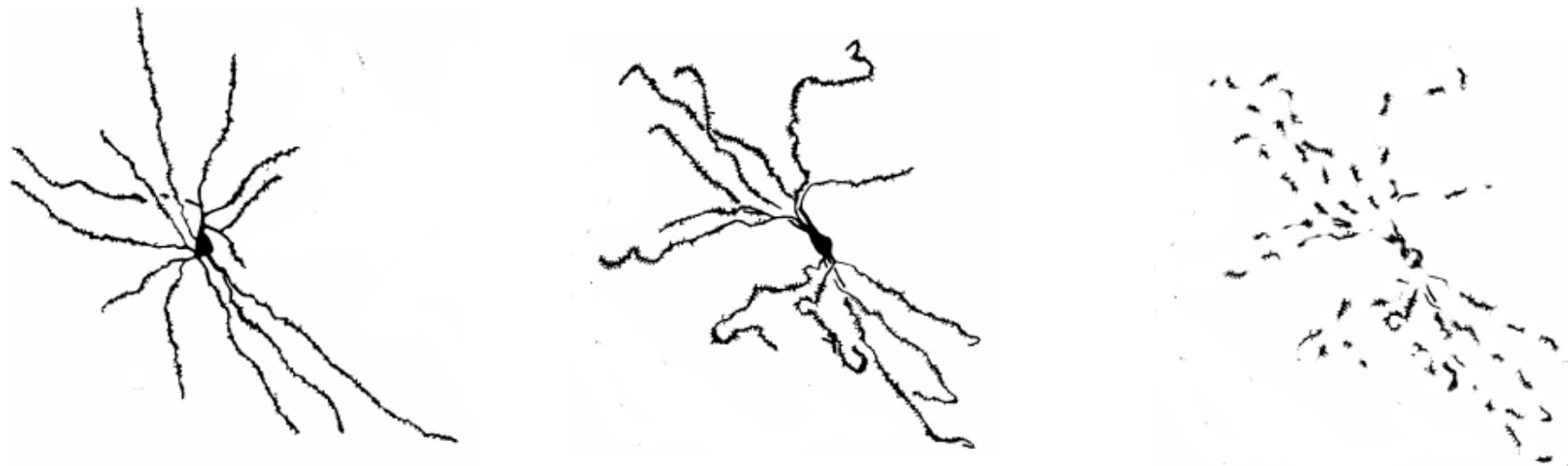
Q **L** C

P All day long, she

S **Y** **h**



Transcription



Mutant huntingtin → → → → → → → → **Death**

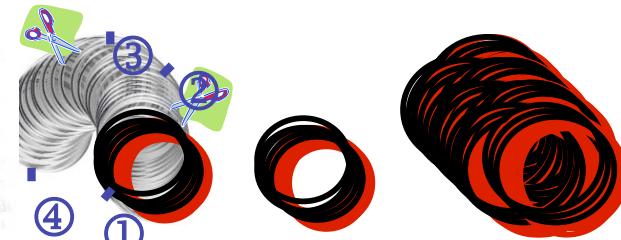
Lifeline of a brain cell with the HD mutation



Trigger mechanism



Changes that may disable the brain cell



Changes related to death of the brain cell



Michael Macor / The Chronicle





